12. Adverse Events Related to Anti-D Immunoglobulin (Anti-D Ig)

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Definition:

An adverse event relating to anti-D Ig is defined as relating to the prescription, administration or omission of anti-D Ig which has the potential to cause harm to the mother or fetus immediately or in the future.

DATA SUMMARY Total number of cases: 249							
Implicated components				**Mortality/morbidity**			
Red cells			0	Deaths *probably/likely* due to transfusion			0
FFP			0	Deaths *possibly* due to transfusion			0
Platelets			0	Major morbidity			9
Anti-D Ig			249	Potential for major morbidity			155
Unknown			0				
Gender		**Age**		**Emergency vs. routine and core hours vs. out of core hours**		**Where transfusion took place**	
Male	1	≥ 18 years	244	Emergency	0	A&E	0
Female	248	16 years to <18 years	3	Routine	0	Theatre	0
Not known	0	1 year to <16 years	2	Not known	249	ITU/NNU/HDU/Recovery	0
		>28 days to <1 year	0			Wards	193
		Birth to ≤28 days	0	In core hours	222	Community	56
		Not known	0	Out of core hours	27	Outpatient / day unit	0
				Not known	0	Not known	0

This section describes the main findings from 236 completed questionnaires. Three questionnaires in the 'wrong dose administered' category refer to 16 separate events, so the total number of cases analysed is actually **249**.

The reports are broken down into the reporting categories shown in Table 12.1.

Under current legislation[48], adverse events related to the administration of anti-D Ig are reportable as 'SHOT-only'. Clinical reactions to anti-D Ig are reportable via the Medicines and Healthcare products Regulatory Agency (MHRA) 'Yellow Card' system.

Table 12.1 Reporting categories

Category of adverse event	Number of cases	
Omission or late administration of anti-D Ig	157	
Inappropriate administration of anti-D Ig	60	
to a RhD positive woman		*30*
to a woman with immune anti-D		*17*
to a mother of a RhD negative infant		*9*
given to the wrong woman		*4*
Wrong dose of anti-D Ig given according to local policy	24	
Handling and storage errors related to anti-D Ig	8	
TOTAL	**249**	

Deaths n=0

There was no reported fetal mortality following the omission or delay in administration of anti-D Ig, though one baby is reported to have died three days after an exchange transfusion given as a result of haemolytic disease of the fetus and newborn (HDFN) - see Case 15.

Major morbidity n=9

There were 2 cases where a mother developed an immune anti-D following delay or omission in prophylaxis during the pregnancy, and a further 7 cases where a positive antibody screen was erroneously assumed by the laboratory to be from prophylaxis, resulting in inadequate monitoring throughout the remaining term of the pregnancies. 6/7 of these cases resulted in babies being born with varying degrees of HDFN and 3/6 required urgent transfusion support.

Potential for major morbidity n=155

In a further 155 cases anti-D Ig was administered more than 72 hours following a potentially sensitising event, or omitted altogether, resulting in the potential for sensitisation of the woman to the D antigen. This satisfies the current SHOT definition of potential major morbidity.

Clinical versus laboratory errors

For the reporting year 2011, 249 events related to anti-D Ig administration are summarised in table 12.2 below, with a breakdown of the proportion of clinical and laboratory errors that were primarily responsible.

The distribution of cases has in past years reflected general SHOT findings that around 2/3 of reports involve errors by clinical staff and 1/3 laboratory staff. This year follows the pattern of 2009 and 2010 with clinical errors accounting for 76% and laboratory errors 24% of the total reports related to administration of anti-D Ig.

Table 12.2 Adverse incidents involving anti-D Ig administration, with site of primary error

Type of event	Cases	Number of primary errors		
		Nurse / midwife	Laboratory	Doctor
Omission or late administration of anti-D Ig	**157**	134	10	13
Anti-D Ig given to RhD positive woman	**30**	18	11	1
Anti-D Ig given to woman with immune anti-D	**17**	6	11	0
Anti-D Ig given to mother of RhD negative infant	**9**	3	6	0
Anti-D Ig given to wrong woman	**4**	4	0	0
Wrong dose of anti-D Ig given	**24**	6	18	0
Anti-D Ig handling & storage errors	**8**	5	3	0
Totals	**249**	**176**	**59**	**14**

Omission or late administration of anti-D Ig n=157

In 134/157 cases the primary error was made by a nurse or midwife, and in 13/157 cases by a doctor. 10/157 errors originated from failures in the laboratory.

37 cases occurred in the community, and 120 in a hospital setting.

As in last year's report, there are multiple examples where anti-D Ig has been issued by the laboratory, only to be found days or weeks later in maternity refrigerators indicating a failure of the discharge checklist, and possibly a lack of understanding by some clinical staff of the time limits within which anti-D Ig must be administered.

Case 1

Anti-D Ig not given following self-referral for per vaginam (PV) bleed

A known RhD negative woman self-referred to the early pregnancy unit following a PV bleed at 14 weeks gestation. The midwife told her she did not need anti-D Ig and sent her home.

Case 2

Failure of communication leads to delay in administration of anti-D Ig

The post-natal ward was telephoned to inform them of maternal and cord results, and that anti-D Ig was available for the woman, details of the call were logged as per standard operating procedure (SOP) in the laboratory. Five days later the laboratory received a telephone call from the community midwife asking if anti-D Ig was required for the woman.

Case 3

Incorrect information given to woman by a junior doctor results in delayed administration of anti-D Ig

A woman presented with a PV bleed at 16 weeks gestation. She was reviewed by the junior doctor, who informed her that she was RhD positive and discharged her. The woman telephoned the early pregnancy unit 4 days later as she had received a leaflet through the post informing her that she was RhD negative.

Case 4

Failure of communication between midwifery teams results in omission of anti-D Ig

There was a failure to record the woman's booking blood results in the notes, and a lack of communication between the Trust midwifery team and the community midwives, resulting in routine antenatal anti-D Ig prophylaxis (RAADP) being omitted completely. The woman presented at delivery having developed an immune anti-D in late pregnancy.

Case 5

Mis-reporting of RhD status leads to omission of RAADP

A laboratory reported equivocal RhD typing results as RhD positive, even though a reference laboratory had confirmed that the woman was a novel D-variant to be treated as RhD negative. As a result, the woman did not receive RAADP or anti-D Ig in response to potentially sensitising events (PSEs) during her pregnancy.

Case 6

Laboratory misunderstands need for anti-D Ig for all PSEs and refuses to issue anti-D Ig

A laboratory refused to issue anti-D Ig following an intrauterine death on the basis that prophylaxis had been given for a potentially sensitising event less than 6 weeks earlier.

Case 7

Lack of knowledge results in delay in administration of anti-D Ig

A woman presented with a PV bleed at 19 weeks gestation, but was discharged without anti-D Ig by a doctor who stated that anti-D Ig should only be given if a Kleihauer test was positive. The woman was recalled and given her anti-D Ig 4 days later.

Case 8

Lack of understanding results in omission of RAADP

Community midwives at a GP surgery returned a dose of anti-D Ig intended for RAADP with the message "already given in hospital". The woman had received prophylaxis in response to a PSE earlier in her pregnancy.

Learning point (repeated from 2010)

- Anti-D Ig must still be administered in response to a PSE* even if the woman has received, or is due to receive, routine antenatal anti-D prophylaxis. RAADP must still be administered at the appropriate time, even if the woman has recently received anti-D prophylaxis for a PSE.

  * PSE = Potentially sensitising event

Inappropriate administration of anti-D Ig n=60

This group is further subdivided into four categories.

Anti-D Ig given to RhD positive women n=30

Overall 19/30 errors were clinical, 18 made by a nurse or midwife and 1 by a doctor, and 11/30 primary errors arose in the laboratory.

26/30 errors were made in the hospital setting, with 4 in the community.

Case 9
Anti-D Ig issued to a RhD positive woman after grouping results were mis-transcribed into her notes
Blood grouping results from booking were incorrectly transcribed into a woman's notes and anti-D Ig was issued in response to a sensitising event from stock held in the clinical area.

Case 10
RhD positive woman administered RAADP after results were incorrectly entered onto IT system
Blood grouping results from booking had been incorrectly entered (manually) onto the maternity computer system. As a result, the woman was given 1500 iu anti-D Ig from clinical stock as RAADP.

Case 11
Laboratory telephone incorrect result to the clinical area
A biomedical scientist telephoned an incorrect grouping result to the ward, then failed to notice the discrepancy on the laboratory computer system when requested to issue anti-D Ig for the woman.

Case 12
Misinterpretation of blood grouping report results in inappropriate administration of anti-D Ig
A junior doctor misread a woman's grouping report, and interpreted the negative antibody screen as the RhD-type. Anti-D Ig was erroneously issued to the woman from stock held in the clinical area.

Case 13
Anti-D Ig requested from Pharmacy
The clinical area requested anti-D Ig directly from Pharmacy, bypassing any grouping checks, and administered it to a RhD positive woman.

Anti-D Ig given to women with immune anti-D n=17

Of these 17 reported cases 6 resulted from a primary clinical error and 11 from a laboratory error.

15/17 occurred in the hospital setting, with 2/17 in the community.

7/11 of the laboratory errors involved failure to consider that a strongly positive antibody screen could have been from immune anti-D rather than assuming that it must be a result of prophylactic anti-D.

4/11 of the laboratory errors involved failure to take heed of the laboratory computer record that clearly showed the woman to have immune anti-D.

5 clinical errors involved issue of anti-D Ig from stocks held in the clinical area, outside laboratory control.

One clinical error was due to failure to send repeat samples to the laboratory who had reported equivocal results in an antibody screen.

Case 14
Misinterpretation of antibody screen results in lack of monitoring
The laboratory misinterpreted a positive antibody screen as due to prophylaxis, even though there was no record of any being issued or administered. As a result further anti-D Ig was issued, the pregnancy was not closely monitored, and the baby was born suffering from HDFN, requiring 3 blood transfusions to correct severe anaemia.

Case 15

Failure to follow up a weak positive antibody screen results in lack of monitoring

The laboratory staff were unsure whether a weak positive antibody screen was due to prophylaxis. Repeat samples were requested but were not received. As a result further anti-D Ig was issued (correctly, according to guideline), the pregnancy was not closely monitored, mother was reported to have a strong anti-C+D at delivery and the baby was born suffering from HDFN, requiring an exchange transfusion. The baby died three days later.

Case 16

Lack of knowledge results in inappropriate administration of anti-D Ig

A woman was known to have a strong immune anti-D, and there were clear instructions that she did not require prophylaxis. Following an emergency caesarean section, a midwife administered the standard post-natal dose of anti-D Ig from clinical stock.

Anti-D Ig given to mothers of RhD negative infants n=9

3/9 of these errors originated in the clinical area, and 6/9 in the laboratory. All 9 occurred in the hospital setting.

- 3/6 laboratory errors involved inappropriate issue of anti-D Ig by a lone worker biomedical scientist (BMS) out of core hours without referring to the cord grouping results.
- 3/6 laboratory errors involved inappropriate issue when results clearly showed the baby to be RhD negative.
- 3/3 clinical errors involved failure of the checking process during administration.

Case 17

Failure to follow laboratory procedure leads to inappropriate administration of anti-D Ig

A BMS not normally working in transfusion issued anti-D Ig before the baby's group had been fully interpreted. The group was incorrectly recorded manually as RhD positive.

Case 18

Anti-D Ig issued for a PSE, kept on ward then inappropriately administered post delivery

500 iu anti-D Ig had been issued to cover an external cephalic version at 39 weeks. However, it was not given at the time, and kept in a ward refrigerator. It was administered 3 days later following delivery, even though cord results had been telephoned through to the ward as RhD negative.

Anti-D Ig given to the wrong woman n=4

These were exclusively clinical errors, involving failure by nurses or midwives to identify the correct woman.

3/4 cases occurred in the hospital setting, and 1/4 in the community.

Case 19

No identification checks performed

A nurse did not perform any identification checks at all, and administered 250 iu anti-D Ig to the wrong woman following a gynaecological procedure. The woman who received the anti-D Ig was RhD positive.

Case 20

Wrong woman and wrong notes

Anti-D Ig clearly labelled for one woman in a RAADP clinic was administered to a different woman as the midwife failed to carry out basic identification checks. Moreover, the administration was recorded in the intended woman's notes.

Wrong dose of anti-D Ig given n=24

6/24 errors were made by nurses or midwives and 18/24 errors occurred in the laboratory.

14/24 cases occurred in hospital and 10/24 in the community.

Case 21
Incorrect dose of anti-D Ig issued for ten women for RAADP
A trainee BMS issued 10 doses of 1250 iu anti-D Ig instead of 1500 iu doses to cover a RAADP clinic. All doses were administered without question by the clinical staff.

Case 22
Misreading of a Kleihauer film results in administration of 10 times the correct dose of anti-D Ig
A BMS reported a transplacental haemorrhage (TPH) of 40mL, for which a 5000 iu dose of anti-D Ig was issued and administered.
The film was reviewed by a senior member of staff the following day - no fetal cells were detected at all, and a 500 iu standard post-natal dose would have been sufficient.

Case 23
Misreading of a Kleihauer film results in significant under-dosing with anti-D Ig
A BMS reported a 6.5mL TPH, and issued 1000 iu anti-D Ig, but did not refer to the Blood Service Laboratory for flow cytometry as it was a weekend. The flow cytometry result showed a TPH of 21.5mL, while another BMS rechecked the Kleihauer film and confirmed this magnitude of bleed. Further anti-D Ig was issued, but later than the 72 hour window.

Case 24
Verbal request leads to inadequate RAADP
Four request forms for anti-D Ig were sent to the laboratory, but contained no clinical details. A midwife gave verbal confirmation that these were all for 500 iu anti-D Ig to cover sensitising events. In fact they were for a RAADP clinic and should have been for 1500 iu each. The discrepancy was not noticed until case notes were reviewed at delivery.

Handling and storage errors related to anti-D Ig n=8

5/8 errors occurred in the clinical area and 3/8 were laboratory errors.

6 errors occurred within a hospital, and 2 in the community.

Case 25
Poor advice from the laboratory results in incorrect route of administration
A BMS advised administering a 1500 iu dose of anti-D Ig intravenously when the product issued was licensed only for intramuscular injection.

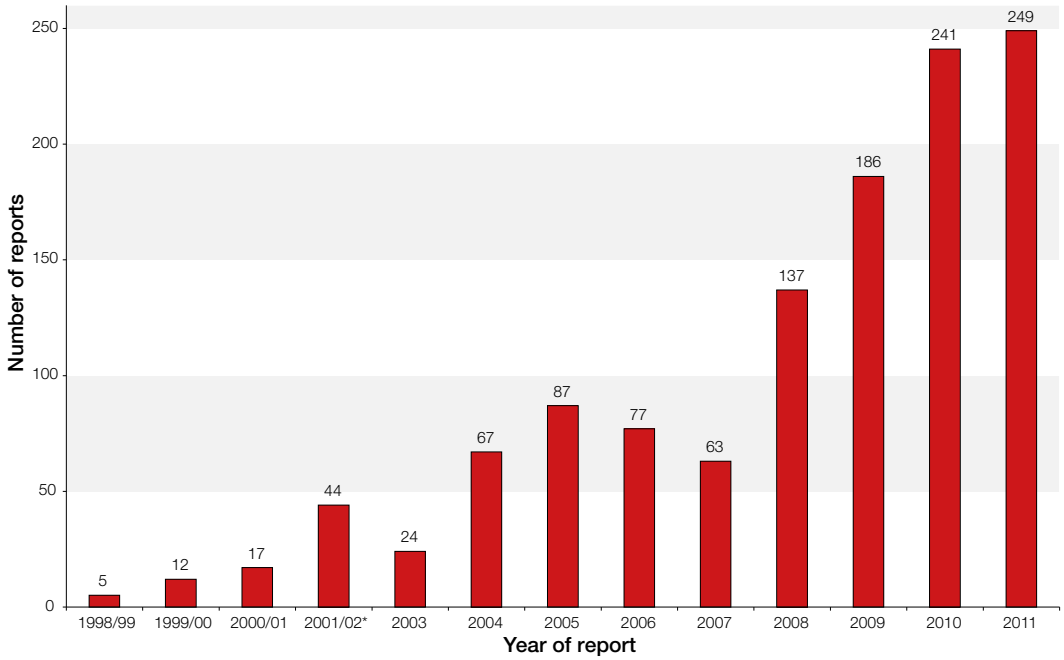
Case 26
Woman administered incorrect globulin
A woman was given 250 iu anti-tetanus globulin by a nurse in the Accident and Emergency (A&E) department, instead of 250 iu anti-D Ig. Both immunoglobulin preparations were kept as stock in the clinical department.

Case 27
Expired anti-D Ig issued from clinical stock
A retrospective review of traceability sheets revealed that expired anti-D Ig had been administered on 3 occasions from remotely held clinical stock.

COMMENTARY

The number of reports reviewed this year was 236, representing 249 individual patients. This represents the maintenance of an upward trend in reporting since SHOT reporting commenced in 1996 (see figure 12.1 below), and is a reflection of an increasing awareness of the need to report rather than a decline in standards of practice.

Figure 12.1
Cumulative data



** 2001–2002 figures covered a 15 month period*

Recurring themes throughout the reports include;

- Communication failures between hospital-based and community-based midwifery teams were cited in 26 cases involving late or omitted anti-D Ig this year.
- The lack of a robust system for receiving and recording anti-D Ig for use at RAADP clinics in the community.
- Failure of the post-natal discharge checklist was cited in 31 cases this year.
- Transcribing blood grouping results onto care plans or the front of notes is not a secure way of recording results, and errors were noted in 9 cases this year.
- Poor decision-making and advice regarding issue and administration of anti-D Ig by laboratory staff lacking relevant knowledge and experience.
- Inappropriate use of anti-D Ig kept in clinical stock (22 cases) or ordered directly from pharmacy (2 cases) outside the control of more robust laboratory procedures.
- Failure to consult the historical group and/or antibody results on the laboratory IT record before issue of anti-D Ig, including issue of anti-D Ig outside the relative security of the laboratory information management system (LIMS). 14 cases could probably have been avoided had available IT information and warning flags been heeded.
- Poor advice given by midwives to women regarding the need for anti-D Ig following sensitising events.
- Clinical staff not reading or misreading laboratory reports before making treatment decisions.
- The inappropriate use of the Kleihauer test by both clinicians and laboratory to decide whether or not anti-D Ig needs to be given in the first place.
- The misinterpretation of Kleihauer films in hospital laboratories leading to errors in dosing with anti-D Ig.
- Failure by both laboratory and clinical staff to follow up women with positive antibody screens detected during pregnancy and an assumption in 7 cases that the result reflected evidence of prophylactic anti-D Ig when none had in fact been administered.

Learning point

- The Kleihauer test provides an approximate measure of fetal red cells in maternal circulation, and is used to determine how much more anti-D Ig than the standard dose, if any, needs to be administered. It is NOT used to determine whether anti-D Ig should be administered in the first place and should not be performed at less than 20 weeks gestation.

2011 is by far the worst year in the history of SHOT with regard to adverse clinical outcome due to errors associated with anti-D Ig. It is disturbing to note 7 cases where the laboratory assumed a positive antibody screen to be due to prophylactic anti-D Ig where in 6 cases there was no record of any prophylactic anti-D Ig being issued, and in 1 case there was a report from a reference laboratory that the woman had immune anti-D. Due to this erroneous reporting there was a lack of clinical follow-up. Six babies were born suffering varying degrees of HDFN, the severity of which may have been mitigated by close monitoring and early intervention. One baby died three days after an exchange transfusion – in this case the clinical area did not respond to requests for repeat samples in order to clarify whether a positive antibody screen was likely to be due to prophylactic or immune anti-D.

Learning points

- Interpretation and reporting of positive antibody screens during pregnancy must be the responsibility of senior laboratory staff, and must take into account an accurate patient history and accurate records of administration of anti-D Ig.
- Effective provision of anti-D Ig prophylaxis is a partnership between the laboratory and the clinical area – the clinical area must be more responsive to requests from the laboratory for follow-up samples and the laboratory must not assume that actions have been taken purely on the basis that a report has been issued.

This year's Annual SHOT Report again highlights a number of key issues in the provision of anti-D Ig, including poor knowledge and understanding in both the laboratory and the clinical area about the use of anti-D Ig, failure to utilise IT to increase the security of the process, and a lack of robust systems for the issue, receipt and recording of anti-D Ig.

Organisations must not be complacent in their arrangements, but should regularly audit the systems in place with a view to improving them, and to this end SHOT has produced a checklist covering key points in the process that may be used as an aide memoire, poster or as an audit tool, and this may be found at http://www.shotuk.org/resources/current-resources/.

While this chapter inevitably concentrates on process failures in the provision of care to a particular group of women, it is apparent that patient choice also plays a role in failures of prophylaxis.

Cases related to patient choice are withdrawn from the final analysis of the Annual SHOT Report as they are outside the control of the transfusion process, but include failure to attend clinic appointments, or refusal to return for administration of anti-D Ig when requested, declining to wait for test results before discharging themselves, and refusal to accept anti-D Ig prophylaxis when offered. One such case of refusal to accept any anti-D Ig during pregnancy resulted in the woman developing a strong immune anti-D and serves as an unfortunate but timely illustration of just how important effective anti-D Ig prophylaxis is.

Recommendations

- All organisations involved in the issue and administration of anti-D Ig must ensure that their systems are robust with respect to issue, receipt and recording, and should audit their systems with a view to increasing the safety and security of the process.
- Kleihauer tests that suggest a transplacental haemorrhage of >2mL, or that give equivocal results, should be referred for flow cytometry at the earliest opportunity.
- Laboratories performing Kleihauer screening must participate in external quality assessment schemes.

Action: Hospital Transfusion Laboratories, Hospital Transfusion Committees, Trust/ Hospital/Health Board Chief Executive Officers (CEOs)

For active recommendations from previous years and an update on their progress, please refer to the SHOT website